

Does inhaled budesonide protect against cardio-ischaeamic events in mild-moderate COPD – a post-hoc evaluation of the EUROSCOP study



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INTRODUCTION

- Numerous epidemiological observations indicate that chronic obstructive pulmonary disease (COPD) is not restricted to the lungs.¹⁻³ A Systemic Inflammatory Syndrome (SIS), triggered by tobacco smoke, may also involve the cardiovascular system resulting in an increased incidence of cardiovascular events.
- It has been shown that one marker of systemic inflammation, C-reactive protein (CRP), has prognostic value not only for cardiovascular diseases but also for COPD.⁴ In addition, evidence suggesting an effect of inhaled corticosteroids on elevated CRP levels has been reported.⁵
- The EUROSCOP study evaluated the effectiveness of long-term (3-year) treatment with the inhaled corticosteroid budesonide in patients with mild COPD who continued smoking.⁶

AIM

- To investigate whether long-term treatment with inhaled budesonide attenuates the incidence of cardio-ischaeamic events, such as angina pectoris and myocardial infarction, in patients with COPD using data from the EUROSCOP study.⁶

METHODS

Patients and design

- The EUROSCOP study was a 3-year, double-blind, randomised, multicentre, placebo-controlled study of budesonide (Pulmicort®) 800 µg/day via Turbuhaler® in patients with mild-moderate COPD.
- Patients 30 to 65 years of age were eligible if they were currently smoking at least 5 cigarettes per day and had smoked cigarettes for at least 10 years or had a smoking history of at least 5 pack-years. Post-bronchodilator forced expiratory volume in 1 second (FEV₁) had to be between 50 and 100% of the predicted normal value, and the ratio of prebronchodilator FEV₁ to slow vital capacity had to be less than 70%. The increase in FEV₁ after the inhalation of 1 mg of terbutaline from a dry-powder inhaler had to be less than 10% of the predicted normal value.
- Subjects with a history of asthma, allergic rhinitis, or allergic eczema and those who had used oral glucocorticoids for more than 4 weeks during the preceding 6 months were excluded.

- The use of inhaled glucocorticoids other than study medication, (β-blockers, cromones, or long-acting inhaled β₂-agonists) was not allowed.

Post-hoc outcome measures

- A hypothesis-based post-hoc analysis was performed using the safety database of the 3-year EUROSCOP study. The System Organ Class (SOC) of adverse events (AE) called *Myo-Endo-, Pericardial & Valve Disorders* contained the following adverse events on Preferred Term (PT) level in the EUROSCOP study: *Angina pectoris, myocardial infarction, coronary artery disorder, cardiomyopathy* and *myocardial ischaemia*. All of these adverse events were considered relevant except *cardiomyopathy*, which was, therefore, excluded prior to the analysis being performed.

Statistical analysis

- The incidence of patients with one or more of the predefined adverse events was calculated and compared between the budesonide and placebo groups. Statistical difference between the groups was assessed by the chi-square test.

RESULTS

- In EUROSCOP a total number of 1175 patients were evaluated for safety, 582 in the placebo group and 593 in the budesonide group. Total number of treatment years were similar, 1505 and 1502 respectively. Discontinuations due to AEs or other reasons were also similar between treatment groups.
- The baseline characteristics of the cardio-ischaeamic patient group were similar to those of the overall population (Table 1).
- Among the 1175 patients, 49 patients (4.2%) had a total of 60 (first-time during study) cardio-ischaeamic events:
 - angina pectoris n=32
 - myocardial infarction n=23
 - coronary artery disorder n=4
 - myocardial ischaemia n=1
- Overall, significantly fewer (p<0.05) patients with one or more cardio-ischaeamic events were receiving budesonide (18/593 patients, 3.0%) compared with placebo-treated patients (31/582 patients, 5.3%)
- The 18 patients in the budesonide group had 22 events, and the 31 placebo treated had 38. The distribution of events are shown in Figure 1.

- Lung function measures and pack-years were similar in patients with cardio-ischaeamic events compared with the overall patient population (Table 1).

Table 1. Baseline demography in patients experiencing a cardio-ischaeamic event compared with the overall patient population

Variable	Cardio-ischaeamic event patients n=49	All EUROSCOP patients n=1175
Males/females, %	84/16	73/27
Age, years	54.8	52.5
Body mass index	25.8	24.8
Pack-years	40	36
FEV ₁ , L	2.50	2.53
FEV ₁ , % of predicted	74.3	76.9
Inspiratory vital capacity, L	4.08	4.09

Abbreviation: FEV₁: forced expiratory volume in 1 second

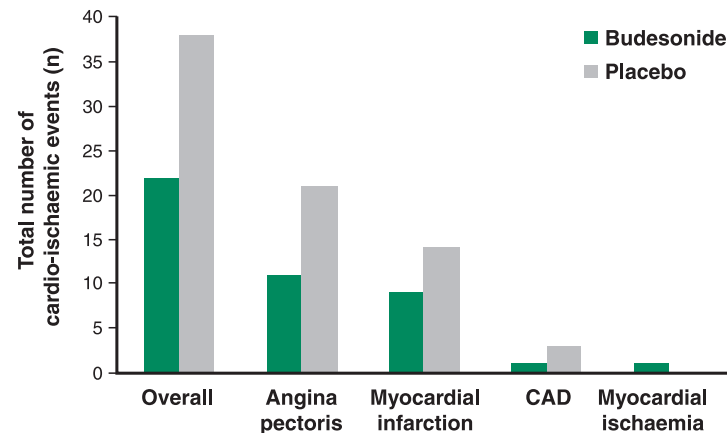


Figure 1. Distribution of cardio-ischaeamic events in patients with COPD receiving budesonide 800 µg/day or placebo for 3 years in the EUROSCOP study. A patient can experience more than one event. CAD: coronary artery disorder.

DISCUSSION

For cardio-ischaeamic events, the long (3-year) duration and a large patient population of the EUROSCOP study is a strength for detecting tentative treatment effects. The findings seem not to be caused by differences between treatment groups regarding duration of exposure to study treatment or withdrawals due to either AEs or other reasons.

CONCLUSIONS

- This post-hoc analysis indicates that treatment with the inhaled corticosteroid budesonide reduces cardio-ischaeamic events in patients with mild-moderate COPD. Further studies are required to verify this finding and to study the mechanisms involved.

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